

Please replace paragraph 201, beginning at page 71, with the following amended paragraph:

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Distinguished from previously characterized coiled-coil leucine zippers from the *Fos* and *Jun* proteins, the C-terminal coiled coil of GABA<sub>B</sub>-R1 and GABA<sub>B</sub>-R2 receptors do not form detectable homodimers under physiological conditions (e.g. *in vivo*); nor do they form homodimers at physiological body temperatures. Research by Kuner *et al.* and White *et al.* (*Science* (1999) 283: 74-77); *Nature* (1998) 396: 679-682)) have demonstrated the heterodimerization specificity of GABA<sub>B</sub>-R1 and GABA<sub>B</sub>-R2 *in vivo*. In fact, White *et al.* were able to clone GABA<sub>B</sub>-R2 from yeast cells based on the exclusive specificity of this heterodimeric receptor pair. *In vitro* studies by Kammerer *et al. supra* has shown that neither GABA<sub>B</sub>-R1 nor GABA<sub>B</sub>-R2 C-terminal sequences is capable of forming homodimers in physiological buffer conditions when assayed at physiological body temperatures (see Table 1 of Kammerer). However, none of these researchers who were involved in the original isolation of the GABA<sub>B</sub>-R2 gene and the characterization of the coiled-coil sequences describe or even suggest the use of this unique heterodimerization sequences for construction of heteromultimers such as antigen-binding units.

**In the Claims:**

Please add new claims 87-93.

87. (New). A non-single-chain antigen-binding unit of claim 1 or 3, wherein said first and second heterodimerization sequences comprise heterodimeric receptor sequences of growth factor receptors.
88. (New). A non-single-chain antigen-binding unit of claim 1 or 3, wherein said first and second heterodimerization sequences comprise heterodimeric receptor sequences of G-protein-coupled receptors.
89. (New). A non-single-chain antigen-binding unit of claim 1 or 3, wherein said first and second heterodimerization sequences comprise heterodimeric receptor sequences of neurotransmitters.
90. (New). A non-single-chain antigen-binding unit of claim 1 or 3, wherein said first and second heterodimerization sequences comprise heterodimeric receptor sequences of nuclear hormone receptors.
91. (New). A non-single-chain antigen-binding unit of claim 1 or 3, wherein the antigen-binding unit is a ccFv fragment.
92. (New). A non-single-chain antigen-binding unit of claim 1, wherein the physiological body temperatures are at about 37°C.
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93. (New) A non-single-chain antigen-binding unit of claim 1, wherein said first and second heterodimerization sequences are essentially incapable of forming homodimers when mixed in equimolar.

Please amend claims 1, 3, 8, 18, 19, 29, 30, 49, 51, 60, 67, 71 as follows:

1. (Amended) A non-single-chain antigen-binding unit comprising:

- (a) a light (L) chain polypeptide comprising a light (L) chain variable region fused in-frame to a first heterodimerization sequence;
- (b) a heavy (H) chain polypeptide comprising a heavy (H) chain variable region fused in-frame to a second heterodimerization sequence;

wherein the L chain and the H chain polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences; and wherein at least one of the heterodimerization sequences is essentially incapable of forming a homodimer under physiological buffer conditions and/or at physiological body temperatures.

3. (Amended) A non-single-chain antigen-binding unit comprising:

- (a) a light (L) chain polypeptide comprising a light (L) chain variable region fused in-frame to a first heterodimerization sequence;
- (b) a heavy (H) chain polypeptide comprising a heavy (H) chain variable region fused in-frame to a second heterodimerization sequence;

wherein the L chain and the H chain polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences, said first and second heterodimerization sequences comprising heterodimeric receptor sequences that mediate heterodimerization of the receptors.

8. (Amended) The non-single-chain antigen-binding unit of claim 4, wherein both the first and the second heterodimerization sequences are linked to at least one cysteine residue.

18. (Amended) The non-single-chain antigen-binding unit of claim 4, wherein the first heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2 and wherein the second heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4, wherein said first and second heterodimerization sequences are linked to cysteine residues.

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19. (Amended) The non-single-chain antigen-binding unit of claim 4, wherein the first heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4; and wherein the second heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2, wherein said first and second heterodimerization sequences are linked to cysteine residues.

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29. (Amended) The single-chain antigen-binding unit of claim 23, wherein the first heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2; and wherein the second heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4, wherein said first and second heterodimerization sequences are linked to cysteine residues.

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30. (Amended) The single-chain antigen-binding unit of claim 23, wherein the first heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4; and wherein the second heterodimerization sequence is a heterodimerization sequence comprising a GABA<sub>B</sub> receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2, wherein said first and second heterodimerization sequences are linked to cysteine residues.

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49. (Amended) A method of producing a non-single-chain antigen-binding unit, comprising:

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- (a) expressing in a host cell a first recombinant polynucleotide encoding a light (L) chain polypeptide comprising a light (L) chain variable region fused in-frame to a first heterodimerization sequence, and a second recombinant polynucleotide encoding a heavy (H) chain polypeptide comprising a heavy (H) chain variable region fused in-frame to a second heterodimerization sequence; wherein the L chain and the H chain polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences; and wherein at least one of the heterodimerization sequences is essentially incapable of forming a homodimer under physiological buffer conditions and/or at physiological body temperatures; and optionally
- (b) isolating the antigen-binding unit expressed in the host cell.

51. (Amended) A method of producing a non-single-chain antigen-binding unit, comprising:

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- (a) expressing in a host cell a first recombinant polynucleotide encoding a light (L) chain polypeptide comprising a light (L) chain variable region fused in-frame to a first heterodimerization sequence, and a second recombinant polynucleotide encoding a heavy (H) chain polypeptide comprising a heavy (H) chain variable region fused in-frame to a second heterodimerization sequence; wherein the L chain and the H chain polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences, said first and second heterodimerization sequences comprising heterodimeric receptor sequences that mediate heterodimerization of the receptors; and optionally
  - (b) isolating the antigen-binding unit expressed in the host cell.

AL6 B3 60. (Amended) The method of claim 56, wherein both the first and the second heterodimerization sequences are linked to at least one cysteine residue.

67. (Amended) A method of producing a non-single-chain antigen-binding unit, comprising:

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- (a) preparing a first recombinant polynucleotide encoding a light (L) chain polypeptide comprising a light (L) chain variable region fused in-frame to a first heterodimerization sequence, and a second recombinant polynucleotide encoding a heavy (H) chain polypeptide comprising a heavy (H) chain variable region fused in-frame to a second heterodimerization sequence; wherein the L chain and the H chain polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences; and wherein at least one of the heterodimerization sequences is essentially incapable of forming a homodimer under physiological buffer conditions and/or at physiological body temperatures; and
  - (b) allowing the first and second polypeptides to dimerize via pairwise affinity of the first and second heterodimerization sequences.

71. (Amended) A method of displaying a chimeric heteromultimer comprising at least two polypeptides on a surface of a host cell, the method comprising: expressing in the host cell

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- (a) a first recombinant polynucleotide encoding a first polypeptide fused in-frame to a first heterodimerization sequence and a surface presenting sequence;
  - (b) a second recombinant polynucleotide encoding a second polypeptide fused in-frame to a second heterodimerization sequence;
- wherein the first and second polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences; wherein at least one of the

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heterodimerization sequences is essentially incapable of forming a homodimer under physiological buffer conditions and/or at physiological body temperatures.